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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,122	02/28/2006	Christine Power	ARS.122	7430

23557 7590 06/15/2011

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
06/15/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slepatents.com

Office Action Summary	Application No.	Applicant(s)	
	10/570,122	POWER ET AL.	
	Examiner	Art Unit	
	REGINA M. DEBERRY	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-50,55 and 57-86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-50,55 and 57-86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The finality of the rejection of the last Office Action (14 January 2011) is withdrawn in view of the rejection set forth below. Please see the Matter of Record section for a summary of the prosecution history and reasons why the prior art of record is not applicable.

Applicant's Request for Reconsideration and Arguments after Final Rejection have been entered (14 April 2011).

Status of Application, Amendments and/or Claims

Claims 1-45, 51-54, 56, are canceled. Claims 46-50, 55, 57-86 are pending and under examination.

Withdrawn Objections And/Or Rejections

The rejection to claims 46-50, 55, 57-86 under 35 U.S.C. 112, first paragraph, scope of enablement, as set forth at pages 2-7 of the previous Office Action (14 January 2011), is *withdrawn* in view of the new rejection below.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-50, 55, 57-86 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The basis for this rejection is set forth at pages 4-7 of the previous Office Action (02 September 2008). The instant rejection is being reinstated for the following reasons.

The specification states that the present invention is in the field of fibrotic diseases/connective tissue disorders and the use of INSP035 for the treatment and/or prevention of fibrotic diseases. The specification teaches the full length cDNA of human INSP035 as SEQ ID NO:1 and the corresponding amino acid sequence as SEQ ID NO:2 (page 9, lines 23-26). The sequence listing teaches SEQ ID NO:2 as having 163 amino acids. The specification teaches the cDNA of human INSP035 starting at the 2nd methionine (called INSP035 medium form) from INSP035 has been cloned. The cDNA is SEQ ID NO:4 and the corresponding amino acid sequence is SEQ ID NO:5 (page 9, lines 26-29). The sequence listing teaches SEQ ID NO:5 as having 88 amino acid residues. The specification teaches that a modified INSP035 medium form with an isoleucine substitution at position 1 has been generated as SEQ ID NO:7 (page 9, lines 29-31). The sequence listing teaches SEQ ID NO:7 as having 88 amino acid residues.

The specification states that the invention is based on the finding that INSP035 is a potent inhibitor of TRAIL in an *in vitro* assay designed to select anti-apoptic molecules in fibroblasts with osteoprotegerin (OPG) as control. The

specification states that like OPG, INSP035 is able to counteract the apoptotic effect of soluble human recombinant TRAIL on fibroblasts, thereby consistently reducing fibroblasts' apoptosis (page 7, lines 1-6). The specification states that administered OPG resulted in significant amelioration of fibrosis in an established animal model of lung fibrosis. The specification states that on the basis that OPG and INSP035 share common functionalities and on the findings that TRAIL stimulates collagen production, INSP035 is suggested to be useful in the treatment of fibrosis (page 8, lines 9-18).

The instant specification cites Taimr et al. (Hepatology, Vol. 37, No. 1, pages 87-95; 2003). The Examiner notes that this particular reference, while cited in the instant specification (page 6, lines 23-28), is not listed on any of the submitted IDS. It is made of record herein. Taimr et al. teach that extensive liver fibrosis, which results from the deposition and accumulation of type I collagen within the liver parenchyma, results in fibrosis. Taimr et al. state that understanding the mechanisms of liver fibrosis is essential to defining anti-fibrotic therapies (page 87, 1st paragraph). Taimr et al. teach that activated hepatic stellate cells (HSCs) have been established as the source of type I and III collagen in the liver. Activated stellate cells secrete type I collagen, the principal matrix protein responsible for the development of liver fibrosis and cirrhosis. Taimr et al. teach that because activated stellate cells are responsible for the exuberant and unbalanced wound healing response in cirrhosis, *their selective removal would be a potential mechanism to attenuate liver fibrosis* (page 87). *Taimr et al. teach that if TRAIL can induce selective apoptosis of activated*

stellate cells, it would become a candidate anti-fibrotic agent. Taimr et al. teach that the present study was to examine the relationship of stellate cells to TRAIL receptors and susceptibility of stellate cells to TRAIL mediated apoptosis (page 88). *Taimr et al. teach that their data suggests that TRAIL agonists could be used to reduce the number of activated stellate cells as a therapeutic approach to reduce fibrosis* (page 94, last paragraph).

Example 2 demonstrates that SEQ ID NO:2 (SEQ ID NO:5 and SEQ ID NO:7) inhibit the TRAIL protein in an in vitro assay. Example 5 is a prophetic teaching suggesting administered SEQ ID NO:2 will protect against lung fibrosis in mice.

The specification teaches ***that INSP035 is able to counteract the apoptotic effect of soluble human recombinant TRAIL on fibroblasts, thereby consistently reducing fibroblasts' apoptosis***. However, Taimr et al. ***teaches the opposite biological affect; that if TRAIL can induce selective apoptosis of activated stellate cells, it would become a candidate anti-fibrotic agent.*** Thus, the instant specification teaches INSP035 as an antagonist of TRAIL, inhibiting TRAIL induced apoptosis to treat fibrosis. ***Conversely,*** Taimr et al. teach that TRAIL agonists would useful in treating fibrosis. The prophetic teaching in Example 5 discloses a model, however based on the teachings of Taimr et al. and the lack of working examples actually demonstrating administered INSPO35 can treat liver or lung fibrosis in vivo, it is highly unpredictable what effect SEQ ID NO: 2, 5, and 7 would have when administered to a patient. The specification need not contain working examples if

the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. However, lack of working examples, is a factor to be considered, especially in cases involving unpredictable and undeveloped art. Such is the instant case. Based on the reasons above, it could not be predicted that the cell culture data presented in the instant specification would be in any way correlative with therapeutic agents for in vivo treatment of fibrotic diseases.

Lastly, the specification fails to teach how to treat a fibrotic disease *in vivo* using fragments and/or mutants of full length INSP035 (SEQ ID NO:2). SEQ ID NO:5 and SEQ ID NO:7 comprise 1/2 the amount of amino acid residues of SEQ ID NO:2. Further, SEQ ID NO:7 comprises a mutation. The disclosure provides no guidance as to which regions of the INSP035 protein would be tolerant of modification and which would not, and it provides no working example of any variant sequence (an actual *in vivo* treatment employing SEQ ID NO:5 and SEQ ID NO:7). The specification fails to teach the structural features that are required in order to provide the biological activity of inhibiting fibrosis. It is extremely complex to predict protein structure from sequence data and in turn utilizing calculated structural determinations to ascertain functional aspects of the protein. For example, the specification states that INSP035 was identified as a leptin (page 5, lines 10-21), but Figure 2 demonstrates that leptin *did not* affect TRAIL-mediated apoptosis, like INSP035 in the *in vitro* assay. Thus, it is in no way predictable that mutations, deletions, etc. in the disclosed sequence would afford a protein having activity comparable to the one disclosed.

Due to the large quantity of experimentation necessary to discern the structural features that are required in fragments and mutants of full length INSP035 (i.e. SEQ ID NO:5 and SEQ ID NO:7) to provide the claimed biological activity of inhibiting fibrosis in vivo, the inherent unpredictability in the field and the lack of guidance in the specification regarding a correlation between the presented in vitro data and the efficacy of administered INSP035 for treating liver or lung fibrosis in vivo, the lack of direction/guidance presented in the specification regarding same and the structural features required to provide the claimed activity, the absence of working examples directed to same, the complex nature of the invention and the state of the art which teaches the opposite biological effect of TRAIL that is needed to treat fibrosis, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

The scientific reasoning and evidence as a whole indicates that the rejection from 08 September 2008 should be reapplied.

MATTER OF RECORD

The Examiner stated (previous Office Action 2/24/09; pages 3-4) that claims 46-50, 55, 57-60 were rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 02/074961 A1). The Examiner stated that Tang et al. teach a polypeptide (SEQ ID NO:913) that is 100% identical to instant SEQ ID NO:2 (See APPENDIX A). The Examiner stated that Tang et al. teach that a composition of the present invention is useful for treatment of lung or liver fibrosis (page 55, lines 24-26).

APPENDIX A

```
GenCore version 6.3
                  Copyright (c) 1993 - 2011  Biocceleration Ltd.


OM protein - protein search, using sw model

Run on:          January  7, 2011, 10:46:43 ; Search time 34 Seconds
                                             (without alignments)
                                             5928.367 Million cell updates/sec

Title:           US-10-570-122A-2
Perfect score:   836
Sequence:        1 MSLGLLKFQAVEEDEEDEE.........LLRHLGLTRMNISARRFTLC 163

Scoring table:   BLOSUM62
                 Gapop 10.0 , Gapext 0.5

Searched:        6395994 seqs, 1224146475 residues

Total number of hits satisfying chosen parameters:      6395994

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :        A_Geneseq_201023:*
                 1:  geneseqp1:*
                 2:  geneseqp2:*
                 3:  geneseqp3:*
                                    SUMMARIES
                  %
Result           Query
   No.   Score  Match Length DB  ID                          Description
 ------------------------------------------------------------------------
     1     836  100.0    163  1  ABU00294                    Abu00294 Human nov

                                   ALIGNMENTS


RESULT 1
ABU00294
ID   ABU00294 standard; protein; 163 AA.
XX
AC   ABU00294;
XX
DT   15-JUN-2007  (revised)
DT   17-JAN-2003  (first entry)
XX
DE   Human novel polypeptide #387.
XX
KW   Human; genetic disorder; gene mapping; medical imaging; cancer;
KW   neurodegenerative disorder; lymphoid cell disorder; osteoporosis;
KW   Parkinson's disease; Alzheimer's disease; bone degenerative disorder;
KW   osteoarthritis; periodontal disease; liver fibrosis; viral infection;
KW   fungal infection; bacterial infection; autoimmune disease; diabetes;
KW   atopic dermatitis; BOND_PC; hypothetical protein MGC10820;
KW   hypothetical protein MGC10820 [Homo sapiens]; MGC10820;
KW   hypothetical protein LOC84734;
KW   hypothetical protein LOC84734 [Homo sapiens]; C1orf90;
KW   chromosome 1 open reading frame 90, isoform CRA_b;
KW   chromosome 1 open reading frame 90, isoform CRA_b [Homo sapiens];
KW   chromosome 1 open reading frame 90;
KW   chromosome 1 open reading frame 90 [Homo sapiens].
XX
OS   Homo sapiens.
XX
PN   WO200274961-A1.
XX
PD   26-SEP-2002.
XX
PF   14-MAR-2002; 2002WO-US005109.
```

```
XX
PR   15-MAR-2001; 2001US-00810173.
XX
PA   (HYSH-) HYSEQ INC.
XX
PI   Tang YT,  Zhou P,  Goodrich R,  Asundi V,  Zhang J,  Zhao QA,  Ren F;
PI   Xue AJ,  Yang Y,  Ma Y,  Yamazaki V,  Chen R,  Wang Z,  Ghosh M;
PI   Wehrman T,  Wang J,  Wang D,  Drmanac RT;
XX
DR   WPI; 2003-040556/03.
DR   N-PSDB; ABX05372.
DR   PC:NCBI; gi110238585.
DR   PC:SWISSPROT; Q9BTA0.
XX
PT   New isolated polypeptides and polynucleotides, useful for preventing,
PT   treating or ameliorating medical conditions, such as cancer,
PT   neurodegenerative disorders, lymphoid cell disorders, bone degenerative
PT   disorders, and infections.
XX
PS   Claim 9; SEQ ID NO 913; 235pp; English.
XX
CC   The invention relates to human polynucleotides and the polypeptides they
CC   encode. The polynucleotides and polypeptides are useful in diagnostics,
CC   forensics, gene mapping, medical imaging, identification of mutations
CC   responsible for genetic disorders or other traits, assessing biodiversity
CC   and producing many other types of data and products dependent on DNA and
CC   amino acid sequences. They are also useful for preventing, treating or
CC   ameliorating medical conditions, such as cancer, neurodegenerative
CC   disorders (e.g. Parkinson's disease, Alzheimer's disease), lymphoid cell
CC   disorders, osteoporosis, osteoarthritis, bone degenerative disorders,
CC   periodontal disease, liver fibrosis, infections (e.g. viral, fungal or
CC   bacterial) or autoimmune diseases (e.g. diabetes, atopic dermatitis).
CC   Sequences ABG99888-ABG99989 and ABU00010-ABU00433 represent human
CC   polypeptides of the invention. Note: The sequence data for this patent is
CC   not represented in the printed specification but is based on sequence
CC   information supplied by the European Patent Office
CC
CC   Revised record issued on 15-JUN-2007 : Enhanced with precomputed
CC   information from BOND.
XX
SQ   Sequence 163 AA;

  Query Match          100.0%;  Score 836;  DB 1;  Length 163;
  Best Local Similarity   100.0%;
  Matches  163;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MSLGLLKFQAVGESDEDEEGESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAWRRAQA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MSLGLLKFQAVGESDEDEEGESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAWRRAQA 60

Qy         61 KPGPGGPGDICGFDSMDSALEWLRRELREMQAQDRQLAGQLLRLRAQLHRLKMDQACHLH 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 KPGPGGPGDICGFDSMDSALEWLRRSLREMQAQDRQLAGQLLRLRAQLHRLKMDQACHLH 120

Qy        121 QELLDSARLELELEPGAGLALAPLLRHLGLTRMNISARRFTLC 163
              |||||||||||||||||||||||||||||||||||||||||||
Db        121 QELLDSARLELELEPGAGLALAPLLRHLGLTRMNISARRFTLC 163
```

Upon further consideration, the Examiner found that Tang et al. does not anticipate the instant claims. The polypeptide corresponding to Tang et al. (SEQ ID NO: 913) is not associated with a polypeptide which can employed for the treatment of liver or lung fibrosis. Tang et al. fail to teach art recognized animal models of fibrosis wherein SEQ ID NO:913 is administered. Further, the Tang reference would require one skilled in the art to pick and choose from various disclosures. The teachings of the Tang reference would not have indicated that the claimed polypeptide should have been used for the treatment of liver or lung fibrosis.

The Examiner provided Appel et al. as a reference of record (previous Office Action 8/12/09; page 5). This was in response to Applicant's arguments that Table 2 (of Tang et al.) indicates that the polypeptide of SEQ ID NO:913 has homology to the human SEC protein of the *sec* oncogene. Applicant cited page Table 2, page 177 of Tang et al. Applicant argued one skilled in the art, in view of the teachings of the reference, would have used the polypeptide associated with SEQ ID NO: 913 in methods of detecting cancers.

Appel et al. (European Journal of Human Genetics Vol. 10:17-25, 2002) teach keratolytic winter erythema (KWE) as an autosomal dominant skin disorder characterized by erythema, hyperkeratosis and peeling of the skin. The chromosomal region has been mapped to human chromosome 8p22-p23. Appel et al. teach to identify candidate genes for KWE, a BAC contig located between the markers at D8S550 and D8S1695 was constructed and sequenced. Twelve transcripts were identified between D8S550 and D8S1759. One transcript

(C8orf13) shows similarity to human SEC oncogene (abstract). Appel et al. teach C8orf13 with an open reading frame of 214 amino acid and shows similarities to the human SEC oncogene (37% in 83 residues)(page 22, last pargraph-1st paragraph, page 23). Appel et al. teach that in order to determine whether one of these transcripts was the KWE gene, exons belonging to a transcript was screened for mutations by sequencing genomic DNA from unaffected individuals and KWE patients (last paragraph, page 23). Appel et al. state that the KWE causing mutation was not identified in any of the transcripts, making it unlikely that one of these is the KWE gene (last paragraph, page 24).

The Examiner incorrectly stated that Appel et al. teach a possible correlation between human SEC protein. Appel et al. teach that as promoters and introns were not analyzed exhaustively, it cannot be excluded that one of the transcripts harbors the pathogenic mutation (last paragraph, page 24).

Listed below are Appendix B and Appendix C. Appendix B is an alignment between instant SEQ ID NOS: 2, 5, and 7 against the sequence referenced in Tang et al. for SEQ ID NO: 913. CAA365502 corresponds to GI36424 (i.e. human sec oncogene for SEC protein; see Table 2 of Tang et al.).

Appendix C (Results #s 1-3) is an alignment between instant SEQ ID NOs:2, 5 and 7 against CAC82740. CAC82740 is the amino acid sequence corresponding to C8orf13 of Appel et al. (see Table 1 of Appel et al., the nucleic acid sequence is Accession No. AJ301564). The final alignment in Appendix C (Result #4) is between CAC82740 (Appel et al.) and CAA36502 (the human sec oncogene sequence referenced by Tang in Table 2 on page 177).

The sequence alignments do not disclose a high percent identity between the instant SEQ ID NOs: and CAA365502 (GI36424 human sec oncogene for SEC protein; Tang et al.) or CAC82740 (C8orf13 of Appel et al.). The sequence alignments do not disclose a high percent identity between CAA365502 and CAC82740.

APPENDIX B

```
GenCore version 6.3
                  Copyright (c) 1993 - 2011  Biocceleration Ltd.


OM protein - protein search, using sw model

Run on:         May  4, 2011, 11:26:12 ; Search time 1 Seconds
                                          (without alignments)
                                          0.037 Million cell updates/sec

Title:              US-10-570-122A-2
Perfect score:  836
Sequence:       1 MSLGLLKFQAVGEEDEEDEE.....LLRHLGLTRMNISARRFTLC 163

Scoring table:  BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched:       1 seqs, 109 residues

Total number of hits satisfying chosen parameters:      1

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :       CAA36502.pep:*

      Pred. No. is the number of results predicted by chance to have a
      score greater than or equal to the score of the result being printed,
      and is derived by analysis of the total score distribution.

                                    SUMMARIES

                 %
Result           Query
   No.   Score  Match Length DB  ID                          Description
 ------------------------------------------------------------------------------
     1     308   36.8    109  1  CAA36502                    Sequence CAA36502


                                   ALIGNMENTS


RESULT 1
CAA36502
; Sequence CAA36502, Application
```

```
; GENERAL INFORMATION
;  APPLICANT:
;  APPLICANT:
;  TITLE OF INVENTION:
;  FILE REFERENCE:
;  CURRENT APPLICATION NUMBER:
;  CURRENT FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  NUMBER OF SEQ ID NOS:
;  SOFTWARE:
; SEQ ID NO CAA36502
;  LENGTH:
;  TYPE:
;  ORGANISM:
CAA36502

  Query Match             36.8%;  Score 308;  DB 1;  Length 109;
  Best Local Similarity   84.7%;  Pred. No. 0;
  Matches   61;  Conservative    5;  Mismatches    6;  Indels    0;  Gaps    0;

Qy          90 MQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG 149
               :|||||||| :||||:|||||:|| ||||||||||||||:||| | || ||| |||||
Db           1 MRAQDRQLAGQPVRLRARLHRLKVDQVCHLHQELLDEAELEMELESGTGLPLAPPLRHLG 60

Qy         150 LTRMNISARRFT 161
               ||||||||||||
Db          61 LTRMNISARRFT 72
```

Title: US-10-570-122A-5

```
Perfect score:  445
Sequence:       1 MDSALEWLRRELREMQAQDR.........LLRHLGLTRMNISARRFTLC 88

Scoring table:  BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched:       1 seqs, 109 residues

Total number of hits satisfying chosen parameters:      1

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :       CAA36502.pep:*

      Pred. No. is the number of results predicted by chance to have a
      score greater than or equal to the score of the result being printed,
      and is derived by analysis of the total score distribution.

                                    SUMMARIES

                 %
Result           Query
  No.   Score  Match Length DB  ID                          Description
 ------------------------------------------------------------------------
    1     308   69.2    109  1  CAA36502                    Sequence CAA36502


                                   ALIGNMENTS


RESULT 1
CAA36502
; Sequence CAA36502, Application
```

```
; GENERAL INFORMATION
;  APPLICANT:
;  APPLICANT:
;  TITLE OF INVENTION:
;  FILE REFERENCE:
;  CURRENT APPLICATION NUMBER:
;  CURRENT FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  NUMBER OF SEQ ID NOS:
;  SOFTWARE:
; SEQ ID NO CAA36502
;  LENGTH:
;  TYPE:
;  ORGANISM:
CAA36502

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  Best Local Similarity   84.7%;  Pred. No. 0;
  Matches   61;  Conservative    5;  Mismatches    6;  Indels    0;  Gaps    0;

Qy         15 MQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG 74
              :||||||||| :||||:|||||:|| ||||||||||||||:||| | || ||| |||||
Db          1 MRAQDRQLAGQPVRLRARLHRLKVDQVCHLHQELLDEAELEMELESGTGLPLAPPLRHLG 60

Qy         75 LTRMNISARRFT 86
              ||||||||||||
Db         61 LTRMNISARRFT 72
```

Title: US-10-570-122A-7

```
Perfect score:  444
Sequence:       1 IDSALEWLRRELREMQAQDR.........LLRHLGLTRMNISARRFTLC 88

Scoring table:  BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched:       1 seqs, 109 residues

Total number of hits satisfying chosen parameters:      1

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries

Database :       CAA36502.pep:*

      Pred. No. is the number of results predicted by chance to have a
      score greater than or equal to the score of the result being printed,
      and is derived by analysis of the total score distribution.

                                    SUMMARIES

Result            %
                  Query
   No.   Score  Match Length DB  ID                          Description
 ------------------------------------------------------------------------
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                                   ALIGNMENTS


RESULT 1
CAA36502
; Sequence CAA36502, Application
```

```
; GENERAL INFORMATION
;  APPLICANT:
;  APPLICANT:
;  TITLE OF INVENTION:
;  FILE REFERENCE:
;  CURRENT APPLICATION NUMBER:
;  CURRENT FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  NUMBER OF SEQ ID NOS:
;  SOFTWARE:
; SEQ ID NO CAA36502
;  LENGTH:
;  TYPE:
;  ORGANISM:
CAA36502

  Query Match             69.4%;  Score 308;  DB 1;  Length 109;
  Best Local Similarity   84.7%;  Pred. No. 0;
  Matches   61;  Conservative    5;  Mismatches    6;  Indels    0;  Gaps    0;

Qy          15 MQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEPGAGLALAPLLRHLG 74
               :|||||||| :||||:|||||:|| ||||||||||||||:||| | || ||| |||||
Db           1 MRAQDRQLAGQPVRLRARLHRLKVDQVCHLHQELLDEAELEMELESGTGLPLAPPLRHLG 60

Qy          75 LTRMNISARRFT 86
               ||||||||||||
Db          61 LTRMNISARRFT 72


Search completed: May  4, 2011, 11:26:12
Job time : 0.259587 secs
```

APPENDIX C

```
                                GenCore version 6.3
                        Copyright (c) 1993 - 2011  Biocceleration Ltd.


OM protein - protein search, using sw model

Run on:         May  4, 2011, 11:39:05 ; Search time 1 Seconds
                                          (without alignments)
                                         0.096 Million cell updates/sec

Title:          CAC82740
Perfect score:  1105
Sequence:       1 MSVPQIHVEEVGAEEGAGAA.....PLKLIGVTKMNISRRFSLC 214

Scoring table:  BLOSUM62
                Gapop 10.0 , Gapext 0.5

Searched:       4 seqs, 448 residues

Total number of hits satisfying chosen parameters:      4

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
                 Maximum Match 100%
                 Listing first 45 summaries
```

```
Database :        seqs:*
                  1:  seqs/CAA36502.pep:*
                  2:  seqs/seqs.pep:*

      Pred. No. is the number of results predicted by chance to have a
      score greater than or equal to the score of the result being printed,
      and is derived by analysis of the total score distribution.

                                    SUMMARIES

                    %
Result              Query
  No.    Score  Match Length DB  ID                          Description
 ------------------------------------------------------------------------
    1   325.5   29.5   163  2  US-10-570-122A-2             Sequence 2, Appli
    2   216.5   19.6    88  2  US-10-570-122A-7             Sequence 7, Appli
    3   213.5   19.3    88  2  US-10-570-122A-5             Sequence 5, Appli
    4   156.5   14.2   109  1  CAA36502                     Sequence CAA36502


                                   ALIGNMENTS


RESULT 1
US-10-570-122A-2
; Sequence 2, Application US/10570122A
; GENERAL INFORMATION
;  APPLICANT: Power, Christine
;  APPLICANT:Lavrovsky, Yan
;  TITLE OF INVENTION: Treatment of Fibrotic Disease
;  FILE REFERENCE: ARS.122
;  CURRENT APPLICATION NUMBER: US/10/570,122A
;  CURRENT FILING DATE: 2006-02-28
;  PRIOR APPLICATION NUMBER: EP 03102723.8
;  PRIOR FILING DATE: 2003-09-08
;  NUMBER OF SEQ ID NOS: 20
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 2
;  LENGTH: 163
;  TYPE: PRT
;  ORGANISM: Homo sapiens
US-10-570-122A-2

  Query Match             29.5%;  Score 325.5;  DB 2;  Length 163;
  Best Local Similarity   34.1%;  Pred. No. 0;
  Matches   73;  Conservative   37;  Mismatches   53;  Indels   51;  Gaps    3;

Qy          1 MSVPQIHVEEVGAEEGAGAAAPPDDHLRSLKALTEKLRLETRRPSYLEWQARLEEHTWPF 60
              ||:  :  : || |:          : | |:|||| ||:|:|||||||| |:::   |
Db          1 MSLGLLKFQAVGEEDEEDEEG---ESLDSVKALTAKLQLQTRRPSYLEWTAQVQSQAW-- 55

Qy         61 PRPAAEPQASLEEGERGGQEPLLPLREAGQHPPSARSASQGARPLSTGKLEGPQSIDEAI 120
                                                | |     |   | : || |:| |:
Db         56 ------------------------------------RRAQAKPGPGGPGDICGPDSMDSAL 80

Qy        121 AWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERDELADL 180
               |||:|| ||: ||:||| ||:||  :::||::  | ||: :|::|  |||
Db         81 EWLRRELREMQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEP----- 135

Qy        181 FCDSPLASSFSLSTPLKLIGVTKMNINSRRFSLC 214
                    :  ::  |: :|:|:|||::|||:||
Db        136 ------GAGLALAPLLRHLGLTRMNISARRFTLC 163


RESULT 2
US-10-570-122A-7
; Sequence 7, Application US/10570122A
; GENERAL INFORMATION
;  APPLICANT: Power, Christine
;  APPLICANT:Lavrovsky, Yan
```

```
;  TITLE OF INVENTION: Treatment of Fibrotic Disease
;  FILE REFERENCE: ARS.122
;  CURRENT APPLICATION NUMBER: US/10/570,122A
;  CURRENT FILING DATE: 2006-02-28
;  PRIOR APPLICATION NUMBER: EP 03102723.8
;  PRIOR FILING DATE: 2003-09-08
;  NUMBER OF SEQ ID NOS: 20
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 7
;  LENGTH: 88
;  TYPE: PRT
;  ORGANISM: Homo sapiens
US-10-570-122A-7

  Query Match             19.6%;  Score 216.5;  DB 2;  Length 88;
  Best Local Similarity   42.4%;  Pred. No. 0;
  Matches   42;  Conservative   24;  Mismatches   22;  Indels   11;  Gaps    1;

Qy        116 IDEAIAWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERD 175
              || |: |||:|| ||: ||:||| |||:||  ::::|||::  | ||: :|::|  |||
Db          1 IDSALEWLRRELREMQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEP 60

Qy        176 ELADLFCDSPLASSFSLSTPLKLIGVTKMNINSRRFSLC 214
                       :  :||  |: :|:|:||||::|||:||
Db         61 ----------GAGLALAPLLRHLGLTRMNISARRFTLC 88


RESULT 3
US-10-570-122A-5
; Sequence 5, Application US/10570122A
; GENERAL INFORMATION
;  APPLICANT: Power, Christine
;  APPLICANT:Lavrovsky, Yan
;  TITLE OF INVENTION: Treatment of Fibrotic Disease
;  FILE REFERENCE: ARS.122
;  CURRENT APPLICATION NUMBER: US/10/570,122A
;  CURRENT FILING DATE: 2006-02-28
;  PRIOR APPLICATION NUMBER: EP 03102723.8
;  PRIOR FILING DATE: 2003-09-08
;  NUMBER OF SEQ ID NOS: 20
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 5
;  LENGTH: 88
;  TYPE: PRT
;  ORGANISM: Homo sapiens
US-10-570-122A-5

  Query Match             19.3%;  Score 213.5;  DB 2;  Length 88;
  Best Local Similarity   41.4%;  Pred. No. 0;
  Matches   41;  Conservative   25;  Mismatches   22;  Indels   11;  Gaps    1;

Qy        116 IDEAIAWLRKELTEMRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERD 175
                 :| |: |||:|| ||: ||:||| |||:||  ::::|||::  | ||: :|::|  |||
Db          1 MDSALEWLRRELREMQAQDRQLAGQLLRLRAQLHRLKMDQACHLHQELLDEAELELELEP 60

Qy        176 ELADLFCDSPLASSFSLSTPLKLIGVTKMNINSRRFSLC 214
                       :  :|:  |: :|:|:|||::||||:||
Db         61 ----------GAGLALAPLLRHLGLTRMNISARRFTLC 88


RESULT 4
CAA36502
; Sequence CAA36502, Application
; GENERAL INFORMATION
;  APPLICANT:
;  APPLICANT:
;  TITLE OF INVENTION:
;  FILE REFERENCE:
;  CURRENT APPLICATION NUMBER:
```

```
;  CURRENT FILING DATE:
;  PRIOR APPLICATION NUMBER:
;  PRIOR FILING DATE:
;  NUMBER OF SEQ ID NOS:
;  SOFTWARE:
; SEQ ID NO CAA36502
;  LENGTH:
;  TYPE:
;  ORGANISM:
CAA36502

  Query Match             14.2%;  Score 156.5;  DB 1;  Length 109;
  Best Local Similarity   37.3%;  Pred. No. 0;
  Matches   31;  Conservative   21;  Mismatches   20;  Indels   11;  Gaps    1;

Qy        130 MRLQDQQLARQLMRLRGDINKLKIEHTCRLHRRMLNDATYELEERDELADLFCDSPLASS 189
                  || ||:||| | :|||  :::||::  | ||: :|:::|  |:|             :
Db          1 MRAQDRQLAGQPVRLRARLHRLKVDQVCHLHQELLDEAELEMELES----------GTG 49

Qy        190 FSLSTPLKLIGVTKMNINSRRFS 212
                 :: ||: :::::|||::|||:
Db         50 LPLAPPLRHLGLTRMNISARRPT 72


Search completed: May  4, 2011, 11:39:05
Job time : 1 secs
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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to REGINA M. DEBERRY whose telephone number is (571)272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/MARIANNE P ALLEN/
Primary Examiner, Art Unit 1647

/R. M. D./
Examiner, Art Unit 1647
5/9/11